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Clinical, epidemiological and socio-cultural aspects of infertility in resource-poor settings. Evidence from Rwanda

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Abstract

Infertility is a serious but entirely neglected public health problem in resource-poor countries. Most of the infertility is caused by infections and therefore potentially preventable. The problem of infertility in Rwanda has not been researched so far.
We examined predictors for infertility and treatment-seeking behaviour in an unmatched case-control. We performed infertility investigations in all infertile couples and discussed consequences of infertility in focus group discussions.
HSV-2 and HIV infection and sexual violence were the most important determinants of infertility. We found a higher HIV prevalence among couples in secondary and not primary infertile relationships with at least one HIV infected partner in 45% of these couples. Men in infertile relationships reported more frequently concurrent partners over the last year than fertile men.
We found a high prevalence of tubal factor (70%) and male factor infertility (64%). Pregnancy rates (16%) were low after conventional therapy.
Both men and women are unlikely to attribute infertility to the male partner. Participants reported a wide array of treatments they received in the past, often including ineffective or even harmful interventions.
We demonstrated severe suffering as a consequence of infertility for both men and women but with women carrying the largest burden, similar to what is reported in other resource-poor countries. Overall, we can conclude that there is an urgent need for a more holistic approach towards reproductive health services in SSA, one that recognises the importance of reproductive failure. The link with HIV has important consequences for both HIV and reproductive health programs.

Key words: Infertility, resource-poor countries, predictors, treatment-seeking behaviour, consequences, HIV.

Introduction

Infertility is an important but entirely neglected public health problem in resource-poor countries. It affects up to one third of couples in certain areas and is causing enormous suffering (Ericksen and Brunette, 1996; Larsen, 2000). At present is has not received the attention it deserves due to limited resources, policies aimed at reducing population growth and the high cost of modern infertility treatment. The problem of infertility in resource-poor countries differs considerably in its causes, management and consequences from resource rich countries.

A WHO multi-centre investigation of 8 500 infertile couples throughout the developed and developing world found that most cases of infertility in African couples are infection-induced and therefore possibly preventable (Cates *et al.*, 1985). Initially fertile women, and to a lesser extent men acquire during their reproductive years ascending reproductive tract infections through sexual transmission, complicated childbirth or unhygienic iatrogenic procedures. Women in resource-poor countries usually do not postpone childbearing, an important factor contributing to the infertility of couples in resource-rich countries, but often their first sexual

contact is followed by a first pregnancy. Therefore secondary infertility is more common than primary infertility, in contrast with the more developed world where primary infertility is the prevailing form (Larsen, 2000). In order to prevent infertility in resource-poor countries the infectious pathogens causing tubal and male infertility and modifiable risk factors related to behaviour and health practices need to be identified. A limited number of studies have shown some evidence that high risk sexual behaviour often starting in adolescence can lead to infertility (Favot *et al.*, 1997; Okumu *et al.*, 1990). *Chlamydia trachomatis* and *Neisseria gonorrhoeae* are thought to be an important cause of pelvic inflammatory disease (PID) and fallopian tube occlusion. Serologic studies in SubSaharan Africa (SSA) have indicated a role of these pathogens in tubal infertility (Biendo *et al.*, 1994; Mabey *et al.*, 1985; Omo-Aghoja *et al.*, 2007; Reniers *et al.*, 1989; Siemer *et al.*, 2008). Other reproductive tract pathogens that have been associated with tubal disease in resource rich countries but not in resource-poor countries are bacterial vaginosis (BV) related organisms and herpes simplex virus type 2 (HSV-2.(Gaudoin *et al.*, 1999; Hettmann *et al.*, 2008).

A couple of studies in SSA have found a higher prevalence of HIV in infertile women and that HIV has a fertility-reducing effect. (Favot *et al.*, 1997; Gray *et al.*, 1998). HIV-positive women (also those with asymptomatic infection) have lower conception rates and higher rates of both early and late pregnancy loss. The lower conception rate is thought to be due to co-infection with sexually transmitted infections (STIs) with resultant tubal factor infertility, weight loss related anovulation and amenorrhoea, male hypogonadism, and impaired spermatogenesis (Adesiyun *et al.*, 2008; Cohen *et al.*, 2005; Crittenden *et al.*, 1992; Dondero *et al.*, 1996; Gray *et al.*, 1998; Kamenga *et al.*, 1995; Lasheeb *et al.*, 1997; Moodley *et al.*, 2002; Muller *et al.*, 1998; Nicopoullos *et al.*, 2004; Temmerman *et al.*, 1992). Many of these mechanisms remain to be elucidated.

In the opposite direction infertility could enhance the spread of HIV through extramarital partners, union dissolutions and unprotected sex which have all been reported more frequently in infertile couples (Barden-O'Fallon, 2005; Favot *et al.*, 1997; Gerrits, 1997; Ikechebelu *et al.*, 2002). The bi-directional link between infertility and HIV deserves special attention because of its obvious consequences for HIV and reproductive health programs.

Over the past three decades the introduction of assisted reproductive technologies (ART) has improved the prognosis for infertile couples in Western countries dramatically and many are seeking – and finding – treatment in the modern infertility services. In the developing world these services are not widely available and its cost makes them inaccessible for most of its inhabitants. Many are either not seeking care or are looking for treatment from all possible sources including traditional healers, spending the little resources they have and rarely with the desired result (Gerrits, 1997; Koster-Oyekan W., 1999; Sundby *et al.*, 1998). One aspect of the management of infertility which can be improved greatly without major costs is information, education and counselling on causes and treatment of infertility and the development and implementation of guidelines for the management of infertility at all levels of healthcare. Knowledge of prevailing perceptions, treatment-seeking behaviour and current practices in the medical sector is needed to guide this process.

To understand the social consequences of infertility in Africa and in most other resource-poor countries it is important to realise that one's place in these societies is defined by the web of relations which are formed with the nuclear and extended family including the dead and the unborn, the village and the nation. Without children this web is cut short. As an individual you have almost non-existing. This is the principle of what is called in Bantu language 'Ubuntu' and means 'I am what I am because of what we are'. This contrasts with classical western thinking where individual freedom and happiness are central values. Therefore consequences of infertility for couples in developing countries, where children are highly valued for economic and socio-cultural as well as personal reasons can be far more severe compared to couples in Western countries. Reports from several African countries, mostly West and South Africa, have documented the overwhelming importance of childbearing and the suffering caused by infertility in these societies (Araoye, 2003; Barden-O'Fallon, 2005; Donkor and Sandall, 2007; Dyer *et al.*, 2002; Dyer *et al.*, 2004; Dyer *et al.*, 2005; Dyer, 2007; Feldman-Savelsberg, 1994; Gerrits, 1997; Hollos, 2003; Hollos *et al.*, 2009; Hollos and Larsen, 2008; Leonard, 2002; Nahar *et al.*, 2000; Richards, 2002; van Balen and Visser, 1997). According to these studies, infertility causes a wide range of psycho-social consequences: loss of marital stability, loss of social status and isolation, loss of social security, problems with gender identity, loss of continuity of family lines and general emotional distress (Dyer, 2007).

Because motherhood is one of the most important ways for African women to enhance their status within the family and the community, childless women often carry the largest burden of the suffering. They may suffer from domestic violence, get abandoned by their partner and may end up as second wife in a polygamous marriage (Araoye,

2003; Dyer *et al.*, 2002; Gerrits, 1997; Ramsay, 1993; van Balen and Gerrits, 2001).

Objectives

Since infertility has not been studied at all in Rwanda this work took an explorative approach studying different aspects of the problem including causes and risk factors, perceptions and treatment seeking behaviour and the socio-cultural consequences of infertility. More specifically we examined predictors and determinants for different types of infertility (female and male factor, primary and secondary infertility) and their relative contribution, including HIV and other reproductive tract infections (RTIs), past sexual and contraceptive behaviour, obstetric history and lifestyle factors. Secondary objectives included the evaluation of perceptions of infertility causes, treatment-seeking behaviour and factors associated with seeking medical care as well as the response of healthcare providers, consequences of female and/or male factor infertility for men and women and the outcome of infertility investigations and 18 month follow-up of infertile women and their partners in Rwanda.

Methodology

Between November 2007 and May 2009 sexually-active women aged 21-45 year presenting with infertility problems at the infertility clinic of the Kigali University Teaching Hospital (KUTH) (n = 312), and fertile controls who recently delivered (n = 312) were surveyed together with their male partners in an unmatched case-control study. Initially, study participants in the infertility arm were recruited among women attending the gynaecological consultations at KUTH and the district hospital of Muhima, the largest secondary referral hospital for gynaecological problems in Kigali. Women enrolled in the study spread the word of the research clinic which resulted in two-thirds of the enrolled participants being recruited through word of mouth. Controls were recruited at the level of the community, as no appropriate control group could be selected at the hospital.

Participants were interviewed about socio-demographic characteristics, medical history, obstetric history, sexual behaviours, sexual functioning and were tested for HIV and RTIs (Table 1). Infertile couples received basic infertility investigations (including hysterosalpingography (HSG) and semen analysis) and locally available conventional treatment (including ovulation induction with Clomiphene Citrate and laparoscopic surgery) and were followed for 18 months.

Table 1. — Overview of all study procedures.

	Infertile women	fertile women	Infertile men	Fertile men
interview	X	X	X	X
HIV serology	X	X	X	X
Syphilis serology	X	X	X	X
HSV-2 serology[a]	X	X	X	X
Wet mount	X	X	X	X
Gram stain	X	X		
NG/CT PCR[b]	X	X		
Chlamydia serology	X	X		
Pap smear		X		
TVUS[c]	X			
HSG[d]**/laparoscopy**	X			
Semen analysis			X	

[a]Herpes Simplex Virus
[b]Neisseria gonorrhoea/Chlamydia trachomatis Polymerase Chain Reaction
[c]Human Papillomavirus
[d]Hysterosalpingography.

In addition five focus group discussions (FGD) were held with selected infertile participants. For each FGD, 7-10 participants were selected from different diagnostic groups: one FGD with women and a second FGD with men from infertile couples diagnosed with female factor only; a third FGD with women and a fourth FGD with men from infertile couples diagnosed with male factor only. This specific group assignment served two purposes: to encourage participant to speak more freely and to explore the effect of gender-specific infertility diagnosis on the experience of infertile couples. A fifth FGD included a mixture of men and women in infertile relationships irrespective of the cause of the infertility.

Results and discussion

Risk factors for infertility

Tubal factor and male factor infertility (Dhont et al., 2010b)

We examined potential predictors and their population attributable fraction (PAF%) for tubal factor and male factor infertility including lifestyle factors, sexual behaviour, and RTIs.

Variables significantly associated with tubal infertility were history of sexual violence (adjusted odds

ratio (AOR) = 2.41; 95%CI = 1.36-4.25); positive HIV (AOR = 2.41; 95%CI = 1.36-4.25), virus type 2 (HSV-2; AOR = 1.67; 95%CI = 1.03-2.71), and *Chlamydia trachomatis* serology (AOR = 1.78; 95%CI = 0.99-3.21), and current BV by Amsel criteria (AOR = 1.97; 95%CI = 1.12-3.47) (Table 1). Among men, male factor infertility was associated with positive HIV (AOR = 2.43; 95%CI = 1.31-5.23) and HSV-2 serology (AOR = 1.71; 95% CI = 1.02-2.87) and current urologic abnormalities (AOR = 2.38; 95%CI = 1.01-5.31). Lifestyle factors such as smoking, alcohol and weight were not related with infertility in our study.

Positive HSV-2 serostatus carried the greatest PAF% (26%) for tubal infertility, followed by positive HIV serostatus (20%) and history of sexual violence (17%). Positive HSV-2 and HIV serology accounted for the largest PAF% for male factor infertility in men (22% and 13% respectively).

In our study, a history of sexual violence contributed more to infertility than other measures of high risk sexual behaviour. It is the first time that a history of sexual violence is found to be associated with infertility. Women in an infertile relationship had experienced three times more sexual violence during their lifetime than fertile women. Although we did not specifically ask, it is possible that many of these women were raped during the genocide of 1994 in Rwanda and it is very likely that levels of sexual violence have decreased considerably since.

The association of HSV-2 with tubal factor infertility but not with non tubal factor infertility in our study suggest that HSV-2 plays a role in tubal pathogenesis. Prior studies in Western countries have shown a possible association between HSV-2 and PID and fallopian tube obstruction, but further research is needed to clarify how HSV-2 contributes to tubal scarring. (Cherpes *et al.*, 2006; Heinonen and Miettinen, 1994; Hettmann *et al.*, 2008; Lehtinen *et al.*, 1985; Paavonen *et al.*, 1985). In our study, HSV-2 was also associated with male factor infertility but not with non male factor infertility, suggesting a causal role of this pathogen in male factor infertility as well.

HIV was consistently associated with all types of infertility in both men and women. The association between infertility and HIV has predominantly been documented in women but much less in men (Adesiyun *et al.*, 2008; Favot *et al.*, 1997; Ikechebelu *et al.*, 2002). Both tubal and non tubal infertility were significantly associated with HIV in our study, but the association with tubal infertility was stronger. Within the infertile women, HIV infection was also significantly associated with tubal pathology. Positive HIV and HSV-2 serostatus could be markers for other past STIs known to be tubal pathogens such as *C.trachomatis* and *G.neisseria*. We could not measure past *G. neisseria* infection. However, the association between HIV and tubal infertility remained significant after adjusting for positive chlamydial antibodies and high risk sexual behaviour, which could be a marker for gonococcus infection. This supports the current hypothesis that HIV plays a role in tubal pathogenesis (Cohen *et al.*, 1998; Kamenga *et al.*, 1995).

The limited role of *C. trachomatis* in infertility in Rwanda is in contrast with findings from Ghana, Gabon, Gambia and Nigeria where Chlamydia antibodies were significantly more often found among infertile women compared to fertile women (Mabey *et al.*, 1985; Omo-Aghoja *et al.*, 2007; Reniers *et al.*, 1989; Siemer *et al.*, 2008). All these studies use different diagnostic assays for identification of Chlamydia antibodies, rendering the comparison of results difficult.

The cross-sectional design of our study limits our ability to ascertain temporal relationships between HIV, HSV-2 and infertility. To further elucidate temporal relationships between infertility and high risk sexual behaviour, STIs and HIV, longitudinal studies of the reproductive and sexual behaviour and incidence of infections in newly married or cohabiting couples are needed.

Another limitation of this study is the possibility of selection bias. The infertile study population is a selection of couples who are willing to undergo infertility investigations; they do not necessarily represent all infertile couples in Kigali.

High risk sexual behaviour, HIV and infertility (Dhont et al., 2011c)

In this study we compared current as well as past high risk sexual behaviour and HIV infection in different groups: men and women in primary infertile relationships, secondary infertile relationships and fertile relationships. The infertile women with a history of a pregnancy in the past (secondary infertile women) and their male partners had very high HIV infection rates (43% and 27% respectively). The secondary infertile women reported high risk sexual behaviour in the past and in the present. This was not the case for primary infertile women who did not differ much in their sexual behaviour and HIV infection rates from fertile women, apart from never use of condoms which is likely to be a result of their infertility, and a higher number of lifetime partners which is in part related to unstable relationships caused by infertility.

Regarding the men, infertility, both secondary and primary was associated with the reporting of extramarital partners over the last year (AOR = 5.4,

Table 2. — Multivariate logistic regression analysis of variables associated with tubal factor infertility(women) and male factor infertility (men).

variable	Women with tubal factor AOR (95% CI)[a]	Men with abnormal semen analysis AOR (95% CI)[a]
Past high risk sexual behaviour[b]	1.43 (0.86-2.39)	NI
Ever exposure to sexual violence	2.41 (1.36-4.25)	NI
HIV serology	2.41 (1.36-4.25)	2.43 (1.31-5.23)
HSV-2 serology	1.67 (1.03-2.71)	1.71 (1.02-2.87)
Chlamydia serology	1.78 (0.99-3.21)	NI
BV (Amsel)	1.97 (1.12-3.47)	NI
Lifestyle[c]	1.18 (0.76-1.82)	NI
Urologic abormaltities	NI	2.32 (1.01-5.31)

[a]AOR = adjusted odds ratio, model includes in addition of all variables listed age, marital status and education
[b]composite variable combining for women: age first intercourse before 15 and/or union dissolutions and/or ever engaged in transactional sex; for men: ever had a marital dissolution and/or age first intercourse before 20 years
[c]composite variable combining using alcohol more than 1 unit a day and/or having BMI >25 and/or ever smoked
BV = bacterial vaginosis.

95%CI = 2.2-12.7; AOR = 7.1, 95%CI = 3.2-15.8, respectively) whereas variables related to sexual behaviour in the past were not very different between the three groups of men.

Our data suggest that secondary infertile women represent a distinct group of infertile women characterised by a risky sexual behaviour profile, often starting in adolescence, which has predisposed them to a first pregnancy, HIV infection, other STIs and subsequent infertility. These first pregnancies occurred in the majority of cases before the age of 21 (55% of secondary infertile women) and were often unwanted (28% of cases). The profile of secondary infertile couples with 45% of the couples having at least one HIV infected partner shows that the epidemics of HIV, STIs, unintended pregnancies and (secondary) infertility are closely linked (Table 2). It can be hypothesised that for primary infertile women it is rather the risky sexual behaviour of their current and/or past sexual partner that has predisposed them to infertility.

Secondary infertility

This study examined the association of factors in the obstetric history and past sexually transmitted infections (STIs) including HIV, BV with secondary infertility and their relative contributions to secondary infertility. For this sub-analysis the cases were women with secondary infertility (n = 177) and the controls were fertile women with at least 2 pregnancies in the past (n = 219) for whom the last pregnancy was not included in the analysis (since these non-pregnant post-partum women have not yet proven their fertility after the last pregnancy). Risk factors in the obstetric history for secondary infertility were lack of prenatal care in the last pregnancy, the first pregnancy before the age of 21 years, a history of unwanted pregnancy, a pregnancy with other than current partner, an adverse pregnancy outcome, stillbirth, postpartum infection and curettage. Presence of HIV, HSV-2, or *Treponema pallidum* antibodies, and BV, were significantly more common in women in secondary infertile relationships than those in fertile relationships (Table 3). The population attributable fractions (PAF%) for obstetric events, HIV, other STIs, and BV were 25%, 30%, 27%, and 14% respectively.

Some previously unknown obstetric history predictors were identified for secondary infertility such as lack of prenatal care during the last pregnancy, unwanted pregnancies and stillbirths. An interesting finding in our study, and not yet reported, is the strong association of unwanted pregnancies with infertility irrespective of a history of induced abortions. Very few infertile women in our study reported induced abortions despite the large number of reported unwanted pregnancies. In a study in Nigeria, induced abortion and post abortion sepsis were the most important risk factors for secondary infertility (Orji, 2008). Induced abortions may have been underreported in our study. To investigate further the circumstances in which the unwanted pregnancy had occurred, all women regardless of study group who had reported an unwanted pregnancy in the past were invited for a semi-structured in-depth interview. 27 out of 63 women reporting an unwanted pregnancy came for the interview, and only one fertile woman

Table 3. — HIV diagnosis on couple level according to fertility status.

Variable	Fertile N = 189 n (%)	Primary infertile N = 119 n (%)	P	Secondary infertile N = 132 n (%)	P
HIV diagnosis on couple level[a]					
Both sero-negative	155 (82)	94 (79)	0.5	73 (55)	< 0.001
Both sero-positive	12 (6)	14 (12)	0.1	27 (20)	< 0.001
Sero-discordant (female +)	16 (8)	6 (5)	0.3	23 (17)	0.02
Sero-discordant (male +)	6 (3)	5 (4)	0.6	9 (7)	0.1

[a]only the couples in which HIV testing was completed are included, 189 women in fertile relationships, 119 women in primary and 132 in secondary infertile relationships.

admitted to an induced abortion that she had not reported in her first structured interview. On the one hand unwanted pregnancies could lead to infertility through lack of prenatal and obstetric care. On the other hand, the unsafe sex which has caused the unwanted pregnancy could also have caused the acquisition of HIV/STIs with secondary infertility as a consequence. Previous studies have demonstrated that women experiencing unwanted births are seeking prenatal care less frequently and are more likely to have a pregnancy complication (preterm birth, perinatal deaths and postpartum infections) (Gipson *et al.*, 2008). We also learned from our in-depth interviews that unwanted pregnancies in women in infertile relationships are often a result of unsafe sex (including sexual violence and sex of younger girl with an older man), and are more likely to result in postpartum infections, although the numbers are too small to draw firm conclusions.

Result of infertility investigations and follow up (Dhont *et al.*, 2011b)

Infertile couples received basic infertility investigations, including HSG and sperm analysis, available treatment was provided and couples were followed up over an 18 month period. The infertility remained unexplained in 3%, was due to a female factor in 31%, due to a male factor in 16%, and due to a combination of male and female causes in 50% of fully investigated couples (n = 224). A tubal factor was found in 69% of women, a male factor in 64% of men. Predictors for tubal infertility in women included a history of high risk sexual behaviour, HIV infection, and a history of STI symptoms in the male partner. After 12-18 months of follow up, 40 pregnancies (16%) had occurred in 244 women. Younger women (age 30 or below) and women with an infertility duration of less than 5 years had a significantly higher chance of becoming pregnant.

Perceptions and treatment seeking behaviour (Dhont *et al.*, 2010a)

When asked about the cause of their infertility, only one in four mentioned explanations based on a medical diagnosis, often they constructed their own medical concept and cited witchcraft or God as the cause of their infertility, despite the fact that the majority (65%) of women had previously been exposed to modern medical health care. There is very little awareness of the link of infertility with high risk sexual behaviour and sexually transmitted infections (STIs). Both men and women are unlikely to attribute infertility to the male partner. Seventy four percent of women and 22% of men had sought care for their infertility in the past. Seeking treatment in the formal medical sector was associated with higher income, being married and infertility duration of more than 5 years in both sexes. In women, higher education and being nulliparous and in men blaming oneself for the infertility was also associated with seeking formal medical care. Women looked for care earlier, more often and from different sources and were more likely to visit traditional healers then men.

Participants reported a wide array of treatments they received in the past, often including ineffective or even harmful interventions. Twenty five percent of women received Clomiphene citrate at least once. Of the 57 women who had received Clomiphene citrate in the past, the majority (49/57, 84%) reported a regular menstrual cycle and in one in three of these women we diagnosed a bilateral tubal block.

In a region where infection-related causes of infertility dominate there is very little awareness of the link of infertility with high risk sexual behaviour and STIs. In our population, very few men and women thought that their infertility could be caused by STIs including HIV. The same was noted by Barden-O'Fallon among women and men in rural Malawi (Barden-O'Fallon, 2005).

Both men and women are unlikely to attribute infertility to the male partner, partly explaining why only 22% of men had ever sought care for infertility. These results are in keeping with reports from other African countries with the exception of South Africa where male infertility awareness was unexpectedly high (Dyer *et al.*, 2004; Fiander, 1990; Sundby, 1997; Sundby *et al.*, 1998). The gender differences which we found in perceptions towards infertility and in treatment seeking behaviour indicate that in Rwandese society the woman is blamed, not only by her partner but also by herself, for the couple's difficulty with childbearing. She carries the greatest burden of stigmatisation and suffering caused by infertility.

In addition to the public services, the private sector and the traditional healer are both important alternative sources of first help. It has been demonstrated repeatedly that traditional healers attract people for infertility treatment (Barden-O'Fallon, 2005; Folkvord, 2005; Stekelenburg *et al.*, 2005; Sundby *et al.*, 1998). Care is often sought from both the traditional and the formal health sector, as is also the case in our population (Dyer *et al.*, 2002). These findings indicate the need to involve healthcare staff from both formal and informal sectors when investing in education of infertile couples and the community about infertility.

Socio-cultural consequences (Dhont *et al.*, 2011a)

Not being able to procreate has severe social and economical repercussions in resource-poor countries. The purpose of this research was to explore the consequences of female and/or male factor infertility for men and women in Rwanda. Both quantitative and qualitative methods were used. Couples were surveyed about domestic violence, current and past relationships and sexual functioning. In addition, five FGDs were held with a subsample of survey participants who were diagnosed with either female or male factor infertility or their partners.

Domestic violence, union dissolutions and sexual dysfunction were reported more frequently by infertile couples (Table 4). Although some couples seem to be able to cope with the burden of infertility and to maintain loving relationships, most FGD participants agreed that 'without children there can be no peace at home', or, 'there can be no love.' Many female FGD participants testified of emotional as well as physical abuse by their partner related to infertility. In the partilineal society of Rwanda it is

Table 4. — Association of obstetrical and reproductive history and reproductive tract infections with secondary infertility.

Variable	Cases N = 177 n (%)	Controls N = 219 n (%)	Age adjusted OR
Obstetrical and reproductive history			
Ever IUCD	2 (1)	5 (2)	0.38 (0.07-2.10)
First pregnancy before age 21 years	97 (55)	92 (42)	2.56 (1.63-4.02)
Unwanted pregnancy	49 (28)	11 (5)	11.51 (5.47-24.20)
Pregnancy with another partner	105 (59)	48 (22)	5.68 (3.56-9.08)
No prenatal care in last pregnancy[a]	20 (15)	7 (4)	4.68 (1.81-12.12)
Unattended birth	44 (25)	75 (34)	0.81 (0.56-1.18)
Adverse pregnancy outcome[b]	57 (32)	44 (20)	1.89 (1.17-3.04)
Stillbirth	32 (18)	6 (3)	7.52 (2.97-19.01)
Unsafe abortion	3 (2)	0 (0)	
Caesarean section	30 (17)	27 (12)	1.33 (0.73-2.39)
Postpartum infection	24 (13)	3 (1)	11.49 (3.31-39.89)
Curettage[c]	32 (18)	23 (10)	1.71 (0.93-3.13)
Reproductive tract infections			
BV	50 (28)	32 (15)	2.68 (1.58-4.54)
Positive HIV serology	74 (42)	35 (16)	4.10 (2.50-6.72)
Positive HSV-2 serology	121 (70)	99 (45)	2.56 (1.65-3.96)
Positive Chlamydia serology	31 (18)	33 (15)	1.58 (0.89-2.80)
Old treated syphilis	16 (9)	8 (4)	2.85 (1.13-7.18)

[a] women whose last pregnancy was a miscarriage are excluded from analysis, leaving 129 cases and 195 controls
[b] includes miscarriage and ectopic pregnancy
[c] includes post-abortion and postpartum curettage.

Table 5. — Relationship characteristics and domestic violence according to fertility status and gender.

	female		
	Fertile N = 312 N (%)	**Infertile N = 312 N(%)**	**p-value**
Ever union dissolution	39 (12)	94 (30)	< 0.001
Ever domestic violence			
Ever been beaten	49 (16)	73 (23)	0.015
Ever been hurt physically	2 (1)	44 (14)	< 0.001
Ever been threatened	20 (6)	54 (17)	< 0.001
Ever been chased	47 (15)	84 (27)	< 0.001
Ever sexual coercion	8 (3)	37 (12)	< 0.001
Partner has other partner			
No	262 (84)	130 (42)	
Don't know	31 (10)	115 (37)	< 0.001
yes	19 (6)	67 (21)	
Extramarital partners at present or last year	3 (1)	9 (3)	0.08
Polygamous union	14 (4)	28 (9)	< 0.001
Sexual intercourse more than 3 times/week	45 (14)	113 (36)	< 0.001
	male		
	N = 189	**N = 254**	
Ever union dissolution	22 (12)	58 (23)	0.002
Partner has other partner			
No	125 (66)	187 (74)	
Don't know	62 (33)	66 (26)	0.19
yes	2 (1)	1 (0)	
Extramarital partners at present or last year	6 (3)	41 (16)	< 0.001
Sexual intercourse more than 3 times/week	26 (14)	95 (37)	< 0.001

the task of the woman to provide her husband's family with offspring, if she can't she is harassed and abused by them. Many FGD participants said that if it were not for the in-laws they would have a good and loving relationship as a couple, despite the infertility. Social security is linked to marital stability for women. The FGDs revealed that husbands sometimes refuse to buy food or clothes for partners with whom they are in an infertile relationship, arguing that 'they don't have any child to give him in return'. Women who are chased away can lose their home, properties and right to utilise the land, which traditionally belongs to the man and his family. Both male and female participants expressed on many occasions the fear "to reach old age with no child to help us". Both men and women in infertile relationships testified of major suffering caused by their community. In fact, some participants said that they would be able to cope with their infertility if it was not for the stigmatization they suffered from the wider community. Only one female and one male FGD participant said that they never experienced any negative consequences of their infertility in the community. One woman said: 'In fact, people with infertility are isolated more than people living with HIV/AIDS.' The men who participated in the FGD worried a lot about the lack of children to continue the family line. Remaining childless means "cutting short the family growth" and also implies that "the dead ancestors cannot be replaced". Both men and women agreed that children are the most important thing in their lives and that, without them, it is very difficult to lead fulfilled and happy lives. Many participants said they would give up all their possessions in exchange for a child. The women more than the men and the women with diagnosed infertility more than the women without a female factor expressed, often in tears, feelings of depression and of being valueless and useless. During the study, many couples received the results of their infertility investigations in each other's presence. Some experiences clearly differed between couples diagnosed with female factor infertility and couples with male factor infertility. Emotional abuse by the partner, including threat of divorce, was mentioned by almost all of the female FGD participants with diagnosed female infertility. The wives of men with male infertility also reported abuse but this abuse generally stopped after

the male factor diagnosis. In contrast, infertile men did not expect to be abandoned by their wives. This was also reported by Horbst in a study of infertile men in Mali (Horbst, 2010). Considering the negative consequences of a female factor diagnosis for women, the question arises whether it is ethical to offer gender-specific diagnosis without the possibility of effective treatment. This applies also to the diagnosis of male factor infertility in the face of which women could be enticed to look for a child outside marriage as was illustrated by the case of one study participant (Mariano, 2004). On the other hand increasing the awareness of male factor infertility has the potential of relieving the burden from women and motivating the men to seek care (Dhont *et al.*, 2010a). The men who participated in our research accepted the diagnosis of male infertility, often after an initial phase of disbelief, and in some cases their behaviour changed towards less abuse of their partner and less extramarital sex.

Conclusions and recommendations

In conclusion, the prevention of HIV and HSV-2 has the potential to prevent an important amount of cases of tubal factor infertility in SSA. Reduced sexual violence and better post rape care has a role to play in infertility prevention, especially in areas with high prevalence of this behaviour. The study on secondary infertility indicated that improved obstetric, neonatal and paediatric care will also have a considerable impact on the rates of infertility and/or childlessness. The high prevalence of past unwanted pregnancies and HIV infection among infertile couples indicates that efforts to prevent infertility should join hands with efforts to prevent HIV and unwanted pregnancies. The safe sex messages used in family planning and HIV programs should teach that unsafe sex does not only increase the risk of acquiring HIV and unintended pregnancies, but can also lead to infertility (Fig. 1).

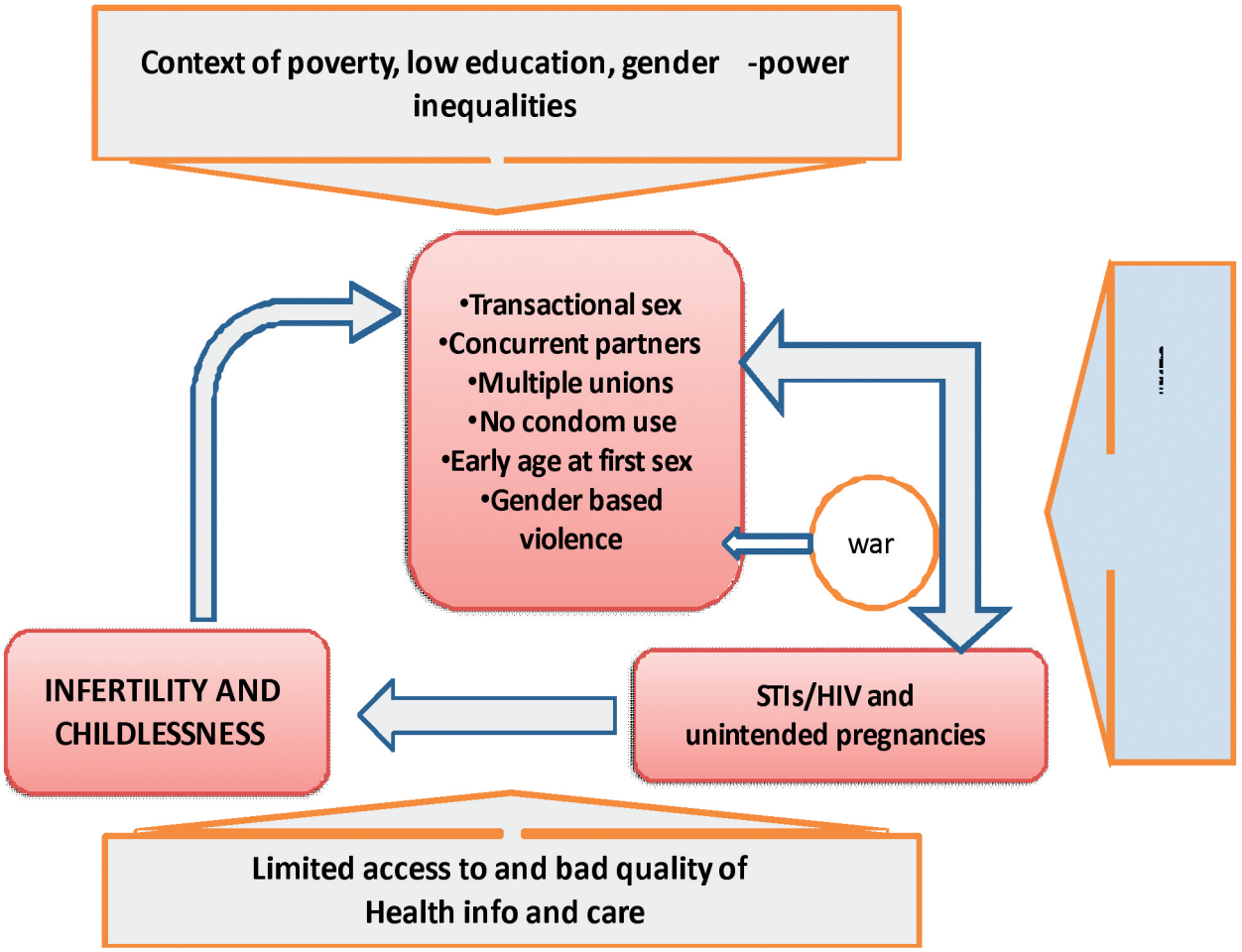

Fig. 1. — Causal pathway of HIV/STIs, unintended pregnancies and infertility

The high HIV prevalence among infertile couples indicate that voluntary HIV counselling and testing of infertile couples may identify new HIV infections and increase opportunities for HIV care and prevention. On the other hand, the link between HIV and infertility represent an opportunity and indeed an obligation to put infertility services in place. Sperm washing techniques can prevent sexual transmission in discordant couples and treating infertile couples effectively can prevent them from spreading HIV infection while 'looking elsewhere' for offspring.

The study of perceptions and treatment-seeking behaviour of infertile couples identified a need to improve information, education and counselling on causes and treatments of infertility. Guidelines for the management of infertility on all levels of healthcare should be drawn up and included in the curriculum of doctors, nurses and midwifes to avoid unnecessary or harmful treatments and to improve counselling on infertility. To increase access to infertility care on a primary care level family planning programs could open their doors for infertile couples.

The psycho-social consequences suffered by infertile couple in Rwanda are severe and similar to those found in other resource-poor countries. Access to and quality of infertility care in Rwanda should be improved to address these problems. Since pregnancy rates are low with conventional therapy a call for affordable IVF in resource-poor countries is made. Fortunately, initiatives to make infertility care accessible in resource-poor settings are gaining momentum (Inhorn, 2003; Inhorn, 2009; Nachtigall, 2006; Ombelet *et al.*, 2008; Ombelet, 2009; Ombelet and Campo, 2007; Vayena *et al.*, 2002; Vayena *et al.*, 2009).

Overall, we can conclude that there is an urgent need for a more holistic approach towards reproductive health services in SSA, one that recognises the importance of reproductive failure and one that provides an integrated package of different services.

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What is already known ?

- More than 80 million couples suffer from infertility, the majority being residents of developing countries.
- Negative consequences of childlessness are experienced to a greater degree in developing countries when compared to Western societies. Childless women are often stigmatised resulting in isolation, neglect, domestic violence and even suicide.
- The most common cause for infertility in developing countries is bilateral tubal occlusion due to sexually transmitted diseases and pregnancy-related infections, a condition that is potentially treatable with assisted reproductive technologies (ART).
- Reduced fecundity in HIV-infected individuals has been described and marital instability and polygamy secondary to infertility may in turn increase the spread of HIV-1 infection.
- New reproductive technologies are, however, either unavailable or very costly in developing countries, and as a result the large majority of the population does not benefit from ART.

What is new from this research ?

- A history of sexual violence, HSV-2 infection and HIV infection are important predictors of infertility in Rwanda
- Obstetric events, HIV and other STIs contribute approximately equally to secondary infertility
- Unsafe sex does not only increase the risk of acquiring HIV and unintended pregnancies, but can also lead to infertility
- Infertile couples should be targeted for HIV prevention progammes and their infertility problems should be addressed, a call for accessible and affordable infertility services
- This PhD shows that there is an urgent need for political willingness to put infertility care on the public health agenda in resource-poor countries.

Which questions will these new findings arise?

- Why do HIV and HSV-2 infections cause infertility? Are these infections associated with tubal damage or is it caused by other STIs
- Do infertile women and men have a higher risk for STIs and HIV due to a different sexual behavior
- How can we convince the local politicians and health care providers to put infertility care on the public health agenda

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